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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,723	06/20/2001	Balasulojini Karunanandaa	MTC 6783.1	3330

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EXAMINER

KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 09/25/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/885,723

Applicant(s)

KARUNANANDAA ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35,38,40,42 and 63-68 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☒ Claim(s) 1-14 is/are allowed.

- 6) ☒ Claim(s) 15-35,38,40,42 and 63-68 is/are rejected.

- 7) ☐ Claim(s) _____ is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13 1/2
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 36, 37, 39, 41, 43-62 and 69-77 have been cancelled. Claims 1-35, 38, 40, 42 and 63-68 are now pending.

Objection to Claims 1, 6, 12, 18, 20, 25-29 is withdrawn in view of Applicant's amendments.

Objection to Claims 40 and 42 is withdrawn in view of Applicant's amendments.

Rejection of Claims 1-35, 38, 40, and 42 under 35 U.S.C. 112, first paragraph, written description is withdrawn in view of Applicant's arguments.

Rejection of Claims 1-14 under 35 U.S.C. 112, first paragraph, enablement, is withdrawn in view of Applicant's arguments.

Rejection of Claims 20-24 and 26 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicant's amendments and arguments.

Rejection of Claims 15, 17-19, 31-35 and 67-68 under 35 U.S.C. 101 is withdrawn in view of Applicant's amendments.

Rejection of Claims 1-35, 38, 40 and 42 under 35 U.S.C. 103(a) is withdrawn in view of Applicant's arguments.

Claim Rejections - 35 USC § 112

Claims 63-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 3/27/2003. Applicant's arguments filed 6/30/2003 have been considered but are not deemed persuasive.

Applicant asserts that S-adenosylmethionine-dependent gamma tocopherol methyltransferase is disclosed and claimed in WO 00/61771 (response page 8, lines 4-6). A review of the cited reference reveals only one DNA sequences encoding S-adenosylmethionine-dependent gamma tocopherol methyltransferase from *Arabidopsis* and another from the bacterium *Synechocystis* on Page 108. The references describing the purification of enzymes S-adenosylmethionine-dependent gamma tocopherol methyltransferase from *Capsicum* and *Euglena gracilis* because they contain no sequence information whatsoever. Further, Applicants assertions that the purified enzymes could be sequenced does not indicate whether the enzyme was isolated to sufficient purity to allow for clear amino acid sequence results via Edmund degradation or otherwise. Furthermore, S-adenosylmethionine-dependent gamma tocopherol methyltransferase is a membrane bound enzyme and it is well known in the art that membrane bound proteins are often not isolated successfully.

Applicant has not responded to the rejection of claims 63-64 and 66-67 under written description. Those Claims read upon a multitude of polypeptides which may have the specified activity in addition to other unspecified activities, either related but not specific to tocopherol

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biosynthesis or comprising bifunctional enzymatic properties and hence not easily characterized as a tocopherol biosynthetic enzyme. Further, Applicant has not provided any conserved structural characteristics associated with this claimed invention that would allow for identification of a functional embodiment or allow for the predictable elimination of related sequences that would not embody the invention.

Claims 15-35, 38, 40, 42 and 63-68 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 3/27/2003. Applicant's arguments filed 6/30/2003 have been considered but are not deemed persuasive.

Applicant asserts that Claims 15-19 drawn to storage organs comprising HMG CoA reductase and squalene epoxidase coding DNA are enabled because Examples 1-3 describe plants transformed with recombinant constructs and since the storage organs are produced by said plants they are so too enabled (response page 9 lines 14-17). The claimed recombinant construct comprising both HMG CoA reductase and squalene epoxidase coding DNA are not found in any transformed plant or any transformed storage organ whatsoever. Applicant has not taught a phenotype in the transformed storage organs using the claimed coding sequences of the invention.

Applicant's arguments with respect to enablement have not been directed to S-adenosylmethionine-dependent gamma tocopherol methyltransferase or any unspecified tocopherol biosynthetic enzyme. Applicant simply asserts that the scope of Claims 63-68 is

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narrower and since they are dependent from claims that are enabled then Claims 63-68 are enabled as well (response page 9, lines 18-20). Those claims are not enabled because Applicant was not in possession of the broad category of tocopherol synthesis pathway enzymes or S-adenosylmethionine-dependent gamma-tocopherol methyltransferase as argued supra.

Applicant argues that they have taught a phenotype in a plant transformed with HMG CoA reductase or the catalytic domain of HMG CoA reductase wherein total levels of sterols in seeds were increased in transformed *Arabidopsis* and soybean (response page 10, lines 1-21). However, Applicant has not claimed any specific phenotype.

Applicant asserts an increase in the overall sterol content with a reduction in the campesterol accumulation by 50% in soybean lines transformed with HMG CoA reductase and the coding DNA for sterol methyl transferase II, a steroid biosynthesis enzyme from *Arabidopsis* (response page 10). Applicant has shown increases in sterol content but not with all of the enzymes of the claimed invention.

Applicant asserts that the soybean transformant comprising the HMG CoA reductase had elevated levels of squalene which was surprising (response page 11). Applicant has not taught a phenotype using the coding sequences of the claimed invention.

Applicant has not addressed the physiological constraints raised in the Devarenne article that impose unpredictable limitations upon modification of the pathway as set forth in the claims specifically drawn to plants transformed with a recombinant heterologous plant transformation construct comprising DNA encoding HMG-CoA reductase activity and squalene epoxidase activity or a plant transformed with a recombinant heterologous plant transformation construct

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comprising DNA encoding HMG-CoA reductase activity, squalene epoxidase activity, and SAM methyltransferase activity. That part of the rejection is modified and repeated below.

Moreover, attempts to engineer biosynthetic flux through a pathway by overexpressing several catalytic steps at once would be blocked by other rate limiting enzymatic reactions upstream of the modified pathway steps. Squalene synthase activity is a potential regulatory point in sterol biosynthesis and is active in the pathway prior to the enzymatic conversions catalyzed by squalene epoxidase and SAM methyltransferase of the claimed invention. Interestingly, the enzyme is regulated by protein turnover as well as possibly phosphorylation under elicitor conditions that would normally occur in nature suggesting unpredicted limitations in engineering flux through the sterol biosynthetic pathway (Devarenne T. Plant Physiology, July 2002; Vol. 129, pp. 1095-1106; see Abstract and page 1102 column 2, first full paragraph; the entire paragraph).

Given the lack of guidance for producing plants transformed with a recombinant heterologous plant transformation construct comprising DNA encoding HMG-CoA reductase activity and squalene epoxidase activity or a plant transformed with a recombinant heterologous plant transformation construct comprising DNA encoding HMG-CoA reductase activity, squalene epoxidase activity, and SAM methyltransferase activity, wherein the plants or seeds of the plants have either reduced or increased sterol; the breadth of the claims, and given the unpredictability in the art, undue trial and error experimentation would be needed by one skilled in the art to evaluate the ability of a multitude of genes encoding non-exemplified polypeptides having steroid or tocopherol synthesis pathway activity to alter the sterol/steroid phenotype of a multitude of non-exemplified transformed plant species. Therefore, the invention is not enabled.

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Claims 20-24 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in the rejection.

Claim 20 recites the limitation "said transgenic plant" in line 16. There is insufficient antecedent basis for this limitation in the claim.

Claim 23 recites the limitation "said plant cell" in line 1. There is insufficient antecedent basis for this limitation in the claim.

At Claim 26, line 5, the second "encoding" should be --having--.

Claims 40 and 42 are indefinite for depending upon newly cancelled Claim 37.

Claims 1-14 are allowed.

Claims 63-68 remain and Claims 1-35, 38, 40, 42 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a recombinant vector comprising cDNA encoding an HMG-CoA reductase and a squalene epoxidase; or a HMG-CoA reductase, a squalene epoxidase and an S-adenosylmethionine-dependent gamma tocopherol methyltransferase; and plants transformed with said recombinant constructs.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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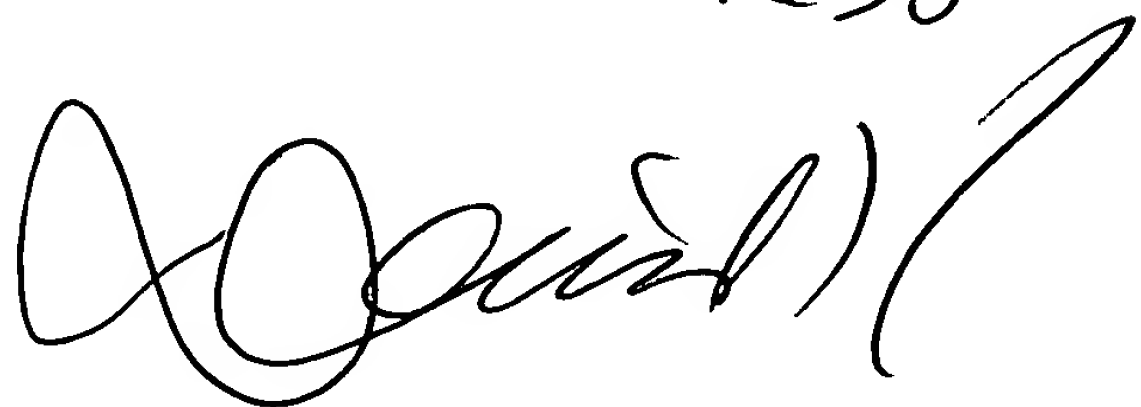
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

Russell Kallis Ph.D.
September 23, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638

A handwritten signature in black ink, appearing to read "David T. Fox", written over the printed name and title.